Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently amended) A method for alleviating a symptom of a neuropsychiatric disorder, the method comprising a step of administering to a patient with a symptom of a neuropsychiatric disorder a therapeutically effective, non-lethal amount of a Clostridial neurotoxin, wherein the Clostridial neurotoxin is locally administered to ~~neural tissue at an intracranial site~~ a site of the brain within the skull of the patient which is associated with the symptom of the neuropsychiatric disorder, thereby alleviating the symptom of the neuropsychiatric disorder.

2. (Original) The method of claim 1, wherein the neurotoxin is made by a bacterium selected from the group consisting of Clostridium botulinum, Clostridium butyricum and Clostridium beratti.

3. (Original) The method of claim 1, wherein the neurotoxin is a botulinum toxin.

4. (Original) The method of claim 3, wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C_1, D, E, F and G.

5. (Original) The method of claim 3, wherein the botulinum toxin is botulinum toxin type A.

6. (Original) The method of claim 3, wherein the botulinum toxin is administered in an amount of between about 10^{-4} U/kg and about 1 U/kg.

7. (Previously presented) The method of claim 1, wherein the symptom alleviation persists for between about 1 month and about 5 years.

8. (Currently amended) The method of claim 1, wherein the ~~neurotoxin is administered to~~ site to which the neurotoxin is administered is a lower brain region.

9. (Currently amended) The method of claim 1, wherein the ~~neurotoxin is administered to~~ site to which the neurotoxin is administered is a pontine region

10. (Original) The method of claim 1, wherein the Clostridial neurotoxin is a recombinantly produced Clostridial neurotoxin thereof.

11. (Currently amended) The method of claim 1, wherein the ~~intracranial~~ administration step comprises implantation of a botulinum toxin containing controlled release system.

12. (Original) The method of claim 1, wherein the administration of the neurotoxin alleviates a symptom of the neuropsychiatric disorder that is associated with hyperactive neurotransmitter release from neurons.

13. (Original) The method of claim 1, wherein administering the Clostridial neurotoxin restores a balance between at least

two neuronal systems that release different neurotransmitters, thereby alleviating the symptom of the neuropsychiatric disorder.

14. (Original) The method of claim 1, wherein administering the Clostridial neurotoxin decreases an acetylcholine release from a cholinergic neuron, thereby alleviating the symptom of the neuropsychiatric disorder.

15. (Original) The method of claim 1, wherein administering the Clostridial neurotoxin decreases a dopamine release from a dopaminergic neuron, thereby alleviating the symptom of the neuropsychiatric disorder.

16. (Original) The method of claim 1, wherein administering of the Clostridial neurotoxin decreases a norepinephrine release from a noradrenergic neuron, thereby alleviating the symptom of the neuropsychiatric disorder.

17. (Currently amended) A method for treating a symptom of a neuropsychiatric disorder, the method comprising a step of administering to a patient with a symptom of a neuropsychiatric disorder a therapeutically effective, non-lethal amount of a botulinum toxin, wherein the botulinum toxin is locally administered to ~~neural tissue at an intracranial site~~ a site of the brain located within the skull of the patient which is associated with the symptom of the neuropsychiatric disorder, thereby treating the symptom of the neuropsychiatric disorder.

18. (Original) The method of claim 17, wherein the botulinum toxin is botulinum toxin type A

schizophrenia a therapeutically effective, non-lethal amount of a botulinum toxin, wherein the botulinum toxin is locally administered to ~~neural tissue at an intracranial site~~ a site of the brain located within the skull of the patient which is associated with a symptom of schizophrenia, thereby treating schizophrenia.

22. (Original) The method of claim 21, wherein the botulinum toxin is botulinum toxin type A

23. (Cancelled)

Application No. 10/421,504, which is directed to methods of treating epilepsy. Claims 1-5, 7-12, 17-18, and 20 have been rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-3 and 5-13 of U.S. Pat. No. 6,620,415, which is directed to methods of treating Parkinson's disease. Claims 1-5, 17-18, and 20 have been rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-3 and 5 of U.S. Pat. No. 6,372,226, which is directed to methods of treating pain. Claims 1-5, 17-18, and 20 have been rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-3 and 13 of U.S. Pat. No. 6,333,037, which is directed to methods of treating pain. Claims 1-5, 17-18, and 20 have been rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-3, 5, 9-17, and 13 of U.S. Pat. No. 6,306,403, which is directed to methods of treating Parkinson's disease.

To advance the prosecution of the above-identified patent application, applicant submits herewith an executed Terminal Disclaimer.

In view of the above, applicant submits that the obviousness-type double patenting rejections have been overcome.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 8-9 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite. In particular, the Office Action states that there is insufficient antecedent basis for claims 8 and 9.

Claims 8 and 9 are dependent from claim 1. Claim 1 has been amended to make more clear that the neurotoxin is locally administered to a site of the brain within the skull of the patient. Claims 8 and 9 define specific sites of the brain within the skull to which the neurotoxin is administered.

Applicant submits that claims 8 and 9 are definite, and have sufficient antecedence basis in claim 1. In other words, claim 1 recites that the neurotoxin is administered to a site of the brain within the skull of a patient, and claims 8 and 9 recite specific sites of the brain. As understood by persons or ordinary skill in the art, lower brain regions and the pontine region are specific regions within the skull of humans. For example, the skull can be understood to comprise three regions: (i) the anterior; (ii) the middle; and (iii) the posterior cranial fossa. The posterior fossa contains the midbrain, the pons, medulla, and the cerebral and cerebellar hemispheres (e.g., see page 6 of the enclosed **Exhibit A**, entitled "Skull Base, Anatomy by Wahan et al., (May 21, 2003)). Thus, applicant submits that the recitation of "a site of the brain within the skull of the patient" in claim 1 provides proper antecedent basis for claims 8 and 9.

In view of the above, applicant submits that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Claim Objections

Claims 8-9 have been objected to under 37 CFR § 1.75(c) as for not further limiting the subject matter of a previous claim (e.g., claim 1).

As discussed above, claim 1 has been amended to recite that the neurotoxin is administered to a site of the brain within the skull of the patient. Claims 8 and 9 further limit the subject matter of claim 1 by identifying specific brain sites to which the neurotoxin is administered.

In view of the above, applicant submits that claims 8 and 9 are in proper dependent form, and that the objections have been overcome, and respectfully requests the objections be withdrawn.

Rejections Under 35 U.S.C. § 102

Claims 1-5, 7-8, 10, and 12-20 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Binder (U.S. Pat. No. 5,714,468). Claims 1-8 and 10-20 remain rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Aoki et al. (U.S. Pat. No. 6,458,365). Claims 1-5, 7, 17-19, and 21-22 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Bassitt et al.

Applicant traverses the rejections as it relates to the present claims.

Each of the presently claimed methods recite that the Clostridial neurotoxin is locally administered to a site of the brain within the skull of the patient. Applicant submits that

none of the cited references disclose, teach, or even suggest administering a Clostridial neurotoxin into a site of a brain within the skull of a patient, as recited in the present claims. Therefore, the present claims are not anticipated by, and are unobvious from and patentable over, the prior art under 35 U.S.C. §§ 102 and 103.

It appears the Examiner has interpreted the previous claims to encompass administration of the Clostridial neurotoxin to regions outside of the skull even though the claims stated that the neurotoxin was administered at a site within the skull. To address this apparent confusion, the present claims have been reworded to recite that the neurotoxin is administered to a site of the brain within the skull of a patient. Applicant submits that the cited references do not disclose, teach, or even suggest administration of a Clostridial neurotoxin to a site of the brain within the skull of the patient associated with the symptom of the neuropsychiatric disorder, as recited in the present claims, and as discussed herein.

Applicant maintains and re-submits that the cited references only disclose administration of a botulinum toxin outside of the brain or to a site that is not a part of the brain to treat conditions other than neuropsychiatric disorders.

Binder discloses administration of a botulinum toxin to treat headache pain. The botulinum toxin is administered to regions or sites outside of the brain and skull, such as perimuscular areas of the face, cranium, and neck (column 4, lines 6-18; column 6, lines 49-56; and FIG. 1). Binder further discloses that the most preferred targets sites are the

bilateral temporal, frontal, glabella, and suboccipital areas of the face (column 7, lines 4-6).

Aoki discloses subcutaneous and intramuscular injection of a botulinum toxin to regions or sites outside of the brain and outside of the skull (Example 12).

Bassitt et al. discloses intramuscular injection of botulinum toxin into the eyelids of patient with blepharospasm (uncontrolled blinking). See e.g. page 155, third paragraph of Bassitt et al.. The patient was not administered botulinum toxin to treat a neuropsychiatric disorder, or a symptom thereof, as recited in the present claims. Furthermore, Bassitt does not disclose, teach, or even suggest locally administering a botulinum toxin to a site of the brain. As understood by persons of ordinary skill in the art, eyelids are not sites of the brain.

Applicant submits that none of the cited references disclose, teach, or suggest the present invention. For example, the cited references do not disclose, teach, or even suggest local administration of a Clostridial neurotoxin to a site of the brain within the skull of the patient to treat or alleviate a symptom of a neuropsychiatric disorder, as recited in the present claims.

In contrast, each of the cited references (Binder, Aoki et al., and Bassitt et al.) disclose administration of a botulinum toxin outside of brain and the skull, such as to a muscle located outside of the skull. The references do not disclose, teach, or even suggest administration of a Clostridial neurotoxin to a site of the brain, and furthermore, do not

disclose, teach, or even suggest administration of a Clostridial neurotoxin to a site of the brain located within the skull of the patient, let alone to do so and treat a neuropsychiatric disorder of the patient.

Because the cited references do not disclose each and every limitation recited in the present claims, applicant submits that the present claims cannot be properly anticipated by the references under 35 U.S.C. § 102. Since the cited references disclose administering neurotoxins outside of the brain to treat other conditions, the teachings of the references do not necessarily result in treatment of a symptom of a neuropsychiatric disorder by locally administering a Clostridial neurotoxin to a site of the brain within the skull of a patient, as recited in the present claims. Therefore, the presently claimed methods are not inherent from the teachings of the cited references.

In view of the above, applicant submits that the present claims, that is claims 1-22, are not anticipated by Binder, Aoki et al., or Bassitt et al., under 35 U.S.C. § 102, and that the present claims are unobvious from and patentable over Binder, Aoki et al., or Bassitt et al., taken alone or in any combination, under 35 U.S.C. § 103.

In addition, each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present methods including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.